Citation:

Kabat GC, Cross AJ, Park Y, Schatzkin A, Hollenbeck AR, Rohan TE, Sinha R. Meat intake and meat preparation in relation to risk of postmenopausal breast cancer in the NIH-AARP diet and health study. Int J Cancer. 2009 May 15;124(10):2430-5

PubMed ID: 19165862

Study Design:

prospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To assess the association between meat, meat-cooking methods, and meat-mutagen intake and postmenopausal breast cancer in the NIH-AARP Diet and Health Study cohort

Inclusion Criteria:

For this analysis:

- postmenopausal women: women who reported that their periods had stopped because of natural menopause, surgery, radiation or chemotherapy, women who had had both ovaries or their uterus removed, and women older than 57 years

Exclusion Criteria:

For this analysis:

- subjects who had questionnaires completed by proxy respondents
- prevalent cancer
- death before study entry
- premenopausal women (women who reported they were still menstruating and not taking hormones)
- women with uncertain menstrual status

Description of Study Protocol:

Recruitment: AARP members between 50 and 71 years of age in 1995-1996 recruited in the states of California, Florida, Louisiana, New Jersey, North Carolina and Pennsylvania, and in the metropolitan areas of Atlanta, GA, and Detroit, MI

Design: prospective cohort study

Blinding used (if applicable): N/A

Intervention (if applicable): N/A

Statistical Analysis:

- estimate of means of baseline variables within each quintile of red meat intake
    - for continuous variables - generalized linear models
    - for categorical variables - proportions calculated
- hazard ratios (HR) and confidence intervals (CI): estimated by by Cox proportional hazards model
    - time metric - person-years
        - analyses using age as the time metric gave similar results
    - meat and other dietary variables were energy-adjusted using the density method, with energy included in the model
    - meat intake and meat mutagen variables were categorized into quintiles
        - analyses by deciles also conducted
    - meat intake by cooking method - 4 groups
        - no intake (referent group
        - tertiles of those with > 0 intake
    - tests for trend across categorical variables were calculated using the median values
- multivariate models
    - constructed by individually adding potential confounding variables; retained if:
        - associated with both the disease and exposure,
        - changed the risk estimate by > 10%
    - fully adjusted model included:
        - age
        - body mass index (BMI)
        - height (inches)
        - age at first menstrual period
        - age at first live birth
        - age at menopause
        - number of breast biopsies
        - family history of breast cancer
        - menopausal hormone therapy
        - education
        - race
        - total energy intake (included on a priori basis)
        - saturated fat
        - alcohol intake
        - physical activity
        - smoking
- additional analyses by hormone receptor status
    - available for 47% of estrogen receptor and 45% of progesterone receptor
- association examined of the major meat variables with breast cancer within strata of potential effect modifiers including:
        - BMI

- parity
- menopausal hormone therapy
- smoking
- alcohol consumption
- vegetable intake
- fruit intake
- physical activity

- tests for interaction based on likelihood ratio tests comparing models with and without the product terms representing the variables of interest

- all statistical significance tests were two-sided.

Data Collection Summary:

Timing of Measurements

- Baseline: questionnaires on dietary intake
- 6 months: second dietary questionnaire with meat-cooking module

Dependent Variables

- breast cancer incidence: cases identified by linking cohort members to state cancer registries and to the U.S. National Death Index between 1995 and 2005

Independent Variables

- Dietary intake: semi-quantitative food-frequency questionnaire (FFQ and meat-cooking module; calculated as grams/day
  - total meat
  - red meat
  - white meat
  - processed meat
  - meat cooked at high temperature
    - Quintiles of intake:
  - Q1: $\leq$ 13 grams/day
  - Q2: >13.0 and $\leq$ 21.9 grams/day
  - Q3: > 21.9 and $\leq$ 31.1
  - Q4: > 31.1 and $\leq$ 43.7
  - Q5: > 43.7 grams/day
- meat variables according to cooking method and doneness level: (meat-cooking questionnaire)
  - raw/rare/medium
  - well/very well done
- meat - mutagens: estimated from CHARRED database:
  - HCAs
  - DiMeIQx
  - MeIQx
  - PhIP
  - PAHB[a]P
  - overall meat mutagenic activity

Control Variables

- energy intake
- meat groups and cooking methods
- age
- BMI
- height
- age at first menstrual period
- age at first live birth
- age at menopause
- number of breast biopsies
- family history of brest cancer
- menopausal hormone therapy
- education
- race
- saturated fat intake
- alcohol intake
- physical activity
- smoking

Description of Actual Data Sample:

Initial N:

- N = 120,755 women with complete information
    - number of breast cancer cases identified = 3,818

Age:

- range of mean ages by quintile: 61.8 years to 62.7 years

Ethnicity: not specified

Other relevant demographics: mean of each quintile

Education, college graduate or postgraduate:

- Q1: 39.5%
- Q2: 33.1%
- Q3: 30.1%
- Q4: 27.7%
- Q5: 24.4%

Race, African American

- Q1: 7.2%
- Q2: 5.3%
- Q3: 4.7%
- Q4: 3.9%
- Q5: 3.6%

Anthropometrics: mean of each quintile

BMI (kg/m^2):

- Q1: 25.3
- Q2: 26.2
- Q3: 26.7
- Q4: 27.3
- Q5: 28.1

Height (inches)

- Q1: 64.2
- Q2: 64.3
- Q3: 64.3
- Q4: 64.3
- Q5: 64.2

Location: United States

Summary of Results:

Key Findings:

- Intake of total meat, red meat, and meat cooked at high temperatures showed slight elevations in the HR, some of which reached statistical significance, but without a signficant trend with increasing intake in age-adjusted models or in multivariable models
- Breast cancer risk was not associated with high-temperature cooking methods or level of doneness
- Omitting saturated fat as a covariate and excluding cases diagnosed during the first three years of follow-up did not change the results.
- No significant associations were seen by hormone receptor status for intake of total meat, red meat, meat cooked at high temperatures, or mutageneic activity
- None of the meat or meat mutagen variables was associated with breast cancer within strata of age, BMI, parity, alcohol consumption, smoking, menopausal hormone therapy, or intake of fruits and vegetables
    - there were no significant interactions between the meat variables and these factors

Author Conclusion:

Results of this large prospective study of postmenopausal women do not support the hypothesis that a high intake of meat, red, meat, processed meat, meat cooked at high temperatures, or meat mutagens is associated with increased risk of breast cancer.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes